REMARKS/ARGUMENTS

Upon entry of this amendment, claims 36, 39, 41, and 44 have been amended by this response. Claims 40 and 45 have been canceled. Accordingly, claims 36-39 and 41-44 are pending. Support for the amended claims can be found in the specification. No new matter has been added. Reconsideration is respectfully requested.

Amended Claims

Claims 36, 39, 41, and 44 have been amended. Support for the amended claims can be found in the specification. Specifically, examples for "identifying a mutation in the sample nucleic acid sequence according to at least a ratio and a pattern in the library" can be found at least on page 24-26 of the specification.

Objections

The Examiner objected to claims 36 and 41 for containing typographical errors. More specifically, the word "library" was spelled as "libraray". Applicants submit that the objections for claims 36 and 41 should be withdrawn in light of the amendments made to these claims.

New Matter

Applicants respectfully submit that the incorporation of the priority documents into the specification by Transmittal letter file July 8, 2003 does not constitute new matter within the meaning of 35 U.S.C. §132(a), as the Transmittal letter was filed with the present application and is a part of the original disclosure.

Claim Rejections under 35 U.S.C. §101

Claims 36-40

The Examiner rejected claims 36-40 under 35 U.S.C. §101 for allegedly drawn to non-statutory subject matter. Applicants respectfully traverse these rejections.

The Examiner mistakenly asserted that claims 36-40 are non-statutory because (1) "no actual, concrete result is recited in the claims", (2) "nor is any useful result "produced" in a tangible form." (see page 3 of the Office Action).

With respected to the first condition ("no actual, concrete result is recited in the claims"), the Examiner appears to have misquoted the relevant legal standard. According to the Guideline for Patent Eligible Subject Matter ("the Guideline"), which was cited by the Examiner, to satisfy "the claimed invention otherwise produces a useful, concrete and tangible result"; the Guideline requires concrete result to be produced by the claimed invention, and there is no requirement for actual, concrete result to be recited in the claims.

With regard to the second condition ("nor is any useful result "produced" in a tangible form"), the Examiner seems to have erroneously required that the invention needs to result in "physical transformation of matter". As explained by the Guideline, physical transformation "is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application." (citing *AT&T*, 172 F.3d at 1358-59, 50 USPQ2d at 1452). Furthermore, the Guideline provides that "if the examiner determines that the claim does not entail the transformation of an article, then the examiner shall review the claim to determine if the claim provides a practical application that produces a useful, tangible and concrete result. In determining whether the claim is for a "practical application," the focus is not on whether the steps taken to achieve a particular result are useful, tangible and concrete, but rather that the final result achieved by the claimed invention is "useful, tangible and concrete." Applicants respectfully assert that tangible results are produced. For example, claim 36 recites, *inter alia*, "identifying a mutation in the sample nucleic acid sequence according to at least a ratio and a pattern in the library". Identifying mutation is practical application that is useful, tangible, and concrete. For example, identifying mutation is useful in disease discovery and finding cures thereof.

Therefore, Applicants respectfully assert that claims 36-40 are directed to statutory matters for at least the above reasons.

Claims 41-45

The Examiner rejected claims 41-45 for allegedly being drawn to non-statutory subjected matter, asserting that a program *per se* is non-statutory. The Examiner further alleges that the term "library" is directed to nonfunctional descriptive material. Applicants respectfully traverse these rejections.

Applicants respectfully assert that claims 41-45 are directed to statutory subject matter, and the term "library" is not nonfunctional descriptive material within the language of the Guideline. Claims 41-45 are not program *per se*. More specifically, claims 41-45 are directed to a computer program product stored in a computer-readable medium. As the Guideline explains, "a claimed computer-readable medium encoded with a computer program is a computer element which defines structural and functional interrelationships between the computer program and the rest of the computer which permit the computer program's functionality to be realized, and is thus statutory." See Lowry, 32 F.3d at 1583-84, 32 USPQ2d at 1035.

With respect to the term "library", Applicants respectfully assert that "library" is not nonfunctional descriptive material. As Guideline explains, "USPTO personnel should be prudent in applying the foregoing guidance. Nonfunctional descriptive material may be claimed in combination with other functional descriptive multi-media material on a computer-readable medium to provide the necessary functional and structural interrelationship to satisfy the requirements of 35 U.S.C. Sec. 101. The presence of the claimed nonfunctional descriptive material is not necessarily determinative of nonstatutory subject matter." The "library" as recited in claim 41 stores a plurality of patterns, which are used in combination with program code that "compares a pattern to the plurality of patterns in the library", which to provide a functional and structural interrelationship that can be used for identification of mutation.

Therefore, Applicants respectfully assert that claims 41-45 are directed to statutory matters for at least the above reasons.

Claim Rejections under 35 U.S.C. §112, First Paragraph

Claims 36-45 stand rejected for lack of enablement. More specifically, the Office Action provides three reasons for the rejections. Applicants respectfully disagree, and the reasons are provided below.

The Office Action appears to have misinterpreted the standard for enablement to require recitation of certain features to be included in claims. More specifically, while the Wands factors as cited by the Examiner are relevant in determining whether there is undue experimentation, these factors do not require specific features to be recited in claims. The process of comparing sample sequences as suggested by the Office Action is not necessary to be recited in the claim. In light of the specification, a skill person in the art is able to practice the embodiments of the invention without referring to claims. For example, "claims need no recite...factors where one of ordinary skill...would consider them obvious." *In re Skrivan*, 166 USPQ 85 (CCPA 1970).

The Office Action further alleges that claim 36 is directed to identification of mutation, which is not sufficiently explained in the specification. Further, the Office Action alleges the mutation identification process is not fully explained at pages 45-47 of the specification. Applicants respectfully submit that pages 45-47 do provide sufficient guidance. Moreover, pages 45-47, in conjunction with Figure 15, illustrate the high level flow of one embodiment of the invention. More specific exemplary processes for identification are provided in other sections of the specification. For example, section II of the specification provides an intensity ratio method for identification of mutation, section III provides a reference method for identification of mutation, section IV provides a statistical method for identification of mutation. Therefore, claim 36 is fully enabled by the specification.

The Office Action additionally alleges that claims 36 and 41 are not enabled, as there is no recited relationship between the patterns of nucleic acid sequences and a mutation. Applicants respectfully assert that claims 36 and 41 are enabled, as the abovementioned features are fully described in the specification and are enabled by the relevant sections of the specification. For example statistical method can be used to identify unknown base, which is described in detail in section III of the specification. For example, section III of the specification discloses the following example:

> "The unknown base will be called by comparing the probe intensities of a reference sequence to the probe intensities of a sample sequence. Preferably, the probe intensities of the reference sequence and the sample sequence are from chips

having the same chip wild-type. However, the reference sequence may or may not be exactly the same as the chip wild-type, as it may have mutations.

The bases at the same position in the reference and sample sequences will each be associated with up to four mutation probes and a "blank" cell. The unknown base in the sample sequence is called by comparing probe intensities of the sample sequence to probe intensities of the reference sequence. For example, suppose the chip wild-type contains the sequence 5'-AGACCTTGC-3' and it is suspected that the sample has a possible mutation at the underlined base position, which is the unknown base that will be called by the reference method. The "mutation" probes for the sample sequence may be as follows; 3'-GAAA, 3'-GCAA, 3'-GGAA, and 3'-GTAA, where 3'-GGAA is the wild-type probe.

Suppose further that a reference sequence, which differs from the chip wild-type by one base mutation, has the sequence 5'-AGACATTGC-3' where the mutation base is underlined. The "mutation" probes for the reference sequence may be as follows: 3'-TGAAA, 3'-TGCAA, 3'-TGGAA, and 3'-TGTAA, where 3'-TGTAA is the reference wild-type probe since the reference sequence is known. Although generally the sample and reference sequences were tiled with the same chip wild-type, this is not required, and the tiling methods do not have to be identical as shown by the use of two probe lengths in the example. Thus, the unknown base will be called by comparing the "mutation" probes of the sample sequence to the "mutation" probes of the reference sequence. As before, because each mutation probe is identifiable by the mutation base, the mutation probes' intensities will be referred to as the "base intensities" of their respective mutation bases. As a simple example of one implementation of the reference method, suppose a gene of interest (target) has the sequence 5'-AAAACTGAAAA-3' (SEQ ID NO:4). Suppose a reference sequence has the sequence 5'-AAAACCGAAAA-3' (SEQ ID NO:5), which differs from the target sequence by the underlined base. The reference sequence is marked and exposed to probes on a chip with the target sequence being the chip wild-type. Suppose further that a sample sequence is suspected to have the same sequence as the target sequence except for a mutation at the underlined base position in 5'-AAAACTGAAAA-3' (SEQ ID NO:4). The sample sequence is also marked and exposed to probes on a chip with the target sequence being the chip wild-type. After hybridization and scanning, the following probe intensities (not actual data) were found for the respective complementary probes:

Reference Sample 3'-TGAC -> 12 3'-GACT -> 11 3'-TGCC -> 9 3'-GCCT -> 30 3'-TGGC -> 80 3'-GGCT -> 60 3'-TGTC -> 15 3'-GTCT -> 6

Although each fluorescence intensity is from a probe, the probes may be identified by their unique mutation base so the bases may be said to have the following intensities:

Reference Sample A -> 12 A -> 11 C -> 9 C -> 30 G -> 80 G -> 60 T -> 15 T -> 6

Thus, base A of the reference sequence will be described as having an intensity of 12, which corresponds to the intensity of the mutation probe with the mutation base A. The reference method will now be described as calling the unknown base in the sample sequence by using these intensities."

It is to be appreciated that various detailed description and examples are provided in other sections as well, which fully enable practice of the claimed invention.

Therefore, Applicants respectfully submit that the application fully satisfies the enablement requirement, and thus rejections directed to claims 36-45 under 35 U.S.C. §112, first paragraph should be withdrawn.

Claim Rejections under 35 U.S.C. §112, Second Paragraph

Claims 36-45 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Regarding claims 36 and 41, the Office Action asserts that the term "a pattern" is unclear. Applicants respectfully disagree. Claim 36 and 41 specifically recites that "the pattern corresponding to a region including multiple base positions where probe intensities reflecting hybridization affinity to a reference nucleic acid sequence differ from probe intensities reflecting hybridization affinity to a sample nucleic acid sequence" according certain embodiments of the present invention. Therefore, the term "pattern" is clear and rejections should be withdrawn.

Regarding claims 36 and 41, the Office Action also requests clarification for the term "patterns in a library". Applicants respectfully submit that claims 36 and 41 have been amended to clarify the term.

Regarding claims 37 and 42, the Office Action also requests clarification for the term "destabilization". Applicants respectfully submit that the term is clear by the specification.

For example, destabilization is related to matching of sequences. Merely by way of example, the specification states that "the more destabilizing C-A mismatch results in a larger volume bubble."

Regarding claims 37 and 42, the Office Action also requests clarification for the term "shape of the patterns". Applicants respectfully submit that the term is clear in light of the specification. For example, "shape of the patterns or bubble may indicate what mutation has occurred."

Regarding claims 39 and 44, the Office Action also requests clarification for the limitation "wherein probes corresponding to the probe intensities have a length and an interrogation position". Claims 39 and 44 have been amended accordingly. Claims 39 and 44 both recite that "the base position of the mutation in the sample nucleic acid sequence is identified utilizing the length of the probes and the interrogation position". The limitation is clearly supported by the specification. For example, the specification explains that "the width of the bubble indicates whether there is a false positive, a single mutation or a multiple mutation. If there is a single mutation, the width of the bubble should be approximately equal to the probe length."

Claim rejections for claims 40 and 45 are moot as the two claims are now canceled.

Claim Rejections under 35 U.S.C. §102(e)

The Examiner rejected claims 36-45 under 35 U.S.C. §102(e) for alleged being anticipated by Webster et al. (U.S. Patent No. 6,600,996) ('996 Patent). The Examiner asserted that the '996 Patent benefits from its earliest priority date: October 21, 1994.

Applicants respectfully submit that the rejections based on 35 U.S.C. §102(e) are improper. More specifically, the October 21, 1994 priority date for the '996 Patent is established by the one of the parent applications, application Ser. No. 08/327, 525 ('525 Application). More specifically, the '996 patent is a continuation-in-part of U.S. application Ser. No. 08/529,115, filed Sep. 15, 1995 (now issued as U.S. Pat. No. 6,040,138) and is a continuation-in-part of U.S. application Ser. No. 08/531,137, filed Oct. 16, 1995 (now U.S. Pat. No. 5,974,164, hereinafter

'164 patent), which is a continuation-in-part of U.S. application Ser. No. 08/327,525, filed Oct. 21, 1994 (now U.S. Pat. No. 5,795,716, hereinafter '716 patent).

The Office Action fails to establish that relevant sections of the '996 patent cited against the present application benefit from the priority date of the '525 Application, which should provides priority for some, but not all, of the '996 Patent.

In addition, Applicants would like to point out to the Examiner that the '996 patent and the present application both claim priority from the parent application Ser. No. 08/531,137 ('137 Application).

Claim 36

Assume, *arguendo*, that the '996 Patent may be cited as prior art against the present application, Applicants respectfully submit that the '996 Patent does not teach all the limitations as recited in the amended claims. Among other things, the Examiner needs to show that the '996 Patent teaches "identifying a mutation in the sample nucleic acid sequence according to at least a ratio and a pattern in the library." (emphasis added). As explained by Office Action, in contrast, the '996 Patent appears to teach that mutation are identified using florescence information from probes of specific length at specific location.

For at least the above reasons, claim 36 should be allowed.

Remaining claims

Applicants respectfully submit that the remaining claims should be allowed for substantially the same reason as claim 36, and for specific features they recite.

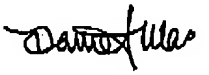
RECEIVED
CENTRAL FAX CENTER
OCT 16 2006

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



Daniel Mao
Reg. No. 51,995

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 650-326-2400
Fax: 415-576-0300

PAGE 19/19 * RCVD AT 10/16/2006 9:01:57 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-3/6 * DNIS:2738300 * CSID:6503262422 * DURATION (mm-ss):05-34